

REMARKS/ARGUMENTS

I. Status of the Claims

After entry of this amendment, claims 1-63 are pending. Claims 8-10 and 15-25 are currently presented. Claims 1-7, 11-14 and 26-48 are withdrawn. Claims 49-63 are new. No claims are cancelled. Claims 8-25 have been amended.

II. The Invention

The present invention provides a family of dendrimers that are useful as, inter alia, supports, vectors, carriers or delivery vehicles for a variety of compounds in biomedical and technological applications. For example, the macromolecules may be used for the delivery of drugs, genetic material, imaging components or other functional molecule to which they can be conjugated. An additional feature of the macromolecules is their ability to be targeted to selected organs, tumors, or types of tissues.

III. The Amendments

Claim 8 is amended in several places. First, the phrase "substantially free of urea side products" has been moved from the preamble to the body of the claim. Since this amendment is correcting a minor error, no support is required for this amendment.

Second, the term "dendrimer" in claim 8 is replaced by the phrase "composition of matter consisting essentially of a plurality of dendrimers". This amendment clarifies that the invention is not a dendrimer motif, but rather a collection of dendrimers in which the collection is substantially free of reaction side products and impurities, such as those derived from carboxyl activating agents. This concept is described in the specification on page 3, lines 3-10.

Third, claim 8 is amended to delete the term "is an active group" from A. "Active groups" in this application refer to moieties which have yet to undergo a chemical reaction in the formation of a dendrimer. Examples of these "active groups" are found on page 22, lines 1-6 of the specification. In contrast, the moiety A in claim 8 has already undergone a chemical reaction

and is thus no longer an 'active group'. Therefore, the deletion of this term is supported by the specification.

All of the claims which are dependent from claim 8 (claims 9-25) have been amended to refer to the "composition of matter" rather than the "dendrimer". Support for these amendments is provided above.

Claims 15 and 16 have been amended in light of a teleconference with Examiner Riley. Please see Section IV for further information.

Amendments have been made to claims 8, 24 and 25 in order to traverse the Examiner's 35 U.S.C. § 112, second paragraph rejections. A discussion of these amendments is included in the traversals below.

IV. The New Claims

New claims 49-63 have been added. These are claims 8-10 and 15-24 rewritten as product by process claims. Support for claims 49-63 are found in original claims 1-48.

V. The Teleconference

Applicants thank Examiner Riley for taking time on Thursday, April 21, 2005 to discuss the Office Action.

During this teleconference, Examiner Riley mentioned that she was considering a rejection of claims 15 and 16. Examiner Riley stated that this rejection would be based upon the Examiner's contention that claims 15 and 16 do not further limit the claim from which they both depend (claim 8). Applicants have therefore amended claims 15 and 16 accordingly.

VI. Responses to the Rejections

Under 35 U.S.C. § 112, second paragraph

Claims 8-10 and 15-25 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.

Claim 8

Claim 8 is rejected for lacking a description of the R³ and R⁴ moieties. Applicants have amended claim 8 to rename R³ and R⁴ moieties as R¹ and R² moieties. Applicants have further amended claim 8 to include descriptions for R¹ and R². Support for this amendment is located from page 16, line 20 to page 17, line 20 of the application. Since Applicants have properly described the terms in claim 8, Applicants respectfully request withdrawal of the rejection.

Claims 24 and 25

Claims 24 and 25 are rejected for lacking a description of the R⁵ and R⁶ moieties. Applicants have amended claims 24 and 25 to include descriptions for R⁵ and R⁶. Support for this amendment is located from page 16, line 20 to page 17, line 20 of the application. Since Applicants have properly described the terms in claims 24 and 25, Applicants respectfully request withdrawal of the rejection.

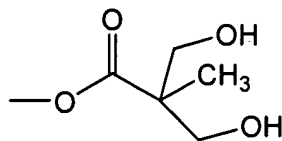
Under 35 U.S.C. § 102

To maintain a *prima facie* case of anticipation, the Examiner must demonstrate that each and every element as set forth in the claim is either expressly found or is inherently described in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the ...claim. See MPEP § 2131. Applicants submit that each element of the claims now pending has not been identified in the art presently of record. Therefore, Applicants respectfully traverse the following rejections.

Under 35 U.S.C. § 102(b)

Over Annby

Claims 8-10 and 17-19 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Annby, *et al.*, *Tetrahedron Letters*, 39: 3217-3220 (1998) ("Annby"). Annby was cited by the Applicants in an earlier filed IDS. Annby is cited by the Examiner for teaching a composition of matter comprising a dendrimer having the following subunit:



In fact, Annby teaches a composition of matter which contains the above dendrimer as well as urea side products. As described below, urea side products include both reaction impurities and reaction by-products. Since urea side products are nearly impossible to completely purify away via filtration, Annby does not teach Applicants element of a urea side product-free composition of matter comprising a dendrimer with a subunit according to Applicants' claim 8. Therefore, an anticipation rejection cannot be maintained.

The Examiner cites structure 2, page 3218 as disclosing Applicants' invention. Structure 2 is produced by a process described on pages 3217-3218.

The synthesis of the 1G (generation) dendrimer **2** commenced by acylation of pentaerythritol. Pentaerythritol (1 eq), acetal (8 eq), DMAP (0.5 eq) and **DCC** (7.5 eq) were allowed to react in methylene chloride at room temperature for 4 days. Removal of **DCU** by filtration followed by washing (NaHCO₃ (aq)), and crystallisation (EtOAc) gave a protected tetraester (8.23 g, 83%).

Annby, page 3217-3218 (emphasis added).

DCC is used in Annby as a coupling agent for the acylation of pentaerythritol.

DCC is known in the art for producing urea side products which are nearly impossible to completely separate away from the desired product via filtration. For example, Radau, *Monatshefte fur Chemie*, **134**, 1033-1036 (2003) ("Radau") discusses the purification problems which plague DCC coupling reactions:

DCC is the most frequently used coupling reagent of the carbodiimide type. In contradiction to this impressive fact, there are several shortcomings to the DCC method. The N,N'-dicyclohexylurea by product, while indeed insoluble in most organic solvents (except alcohols) and thus removable by filtration,

is not entirely insoluble and *therefore it frequently contaminates the product. A more disturbing side reaction* is the intramolecular CO-N shift in the O-acyl isourea intermediate *yielding an N-acylurea derivative as a by-product.*

Radau, p. 1033, (emphasis added)

As mentioned above, purification of a DCC coupling reaction by filtration does not remove all of the urea side products. Urea side products are present in the form of the reaction impurity DCU as well as various N-acylurea dendrimer reaction by-products which have similar molecular weight and compositions as the desired dendrimer product.

While Annby's composition of matter includes a dendrimer which is similar to Applicants, Annby produces this dendrimer via a DCC coupling reaction. Those of skill in the art have noted that DCC coupling reactions produce urea side products which are nearly impossible to completely separate by filtration, which is the purification method used by Annby. No further purification of the urea side products from the desired products are taught by Annby. Therefore, Annby's compositions of matter are not free of urea side products. Annby does not teach Applicants' element of a urea side product-free composition of matter comprising a dendrimer with a subunit according to claim 8. Thus an anticipation rejection can not be maintained, and Applicants' respectfully request withdrawal of the rejection.

Under 35 U.S.C. § 103(a)

In order to establish a *prima facie* case of obviousness, the Examiner must demonstrate that (1) the references teach all the claimed elements; (2) there is a suggestion or motivation in the prior art to modify or combine the reference teachings; and (3) there is a reasonable expectation of success. MPEP § 2143; *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). As explained below, the references fail to disclose or suggest Applicants' claimed element of a urea side-product free composition of matter comprising a dendrimer with a subunit as shown in claim 8. Since the references do not contain this element, there is neither a suggestion to modify the reference teachings to produce Applicants' invention, nor a reasonable expectation of success derived from the references. Therefore, a *prima facie* case of obviousness

has not been put forth for claims 8-10 and 15-25 and Applicants respectfully traverse this rejection.

Over Annby in view of Tomalia

Claim 23 is rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Annby in view of Tomalia (U.S. Pat. No. 5,714,166) ("Tomalia"). As mentioned above, Annby is cited for teaching a composition of matter comprising a dendrimer with a subunit which is allegedly identical to the instant claims. Tomalia is cited by the Examiner for disclosing the use of dendrimers as agricultural or pharmaceutical carriers. As explained below, neither reference discloses nor suggests Applicants' element of a urea side product-free composition of matter comprising a dendrimer with a subunit according to Applicants' claim 8. Since neither Annby nor Tomalia contain this element, there is neither a motivation to combine the reference teachings to produce Applicants' invention, nor can a reasonable expectation of success be derived from the references. Therefore, a *prima facie* case of obviousness cannot be made.

(1) Annby and Tomalia fail to teach all of the claimed elements

As mentioned above, Annby teaches a composition of matter which comprises urea side products and a dendrimer subunit similar to the structure in Applicants' claim 8. The Examiner has cited Tomalia for teaching the use of dendrimers as agricultural or pharmaceutical carriers. The Examiner has not cited Tomalia for teaching a composition of matter which is free of urea side products and comprises a dendrimer subunit similar to the structure in Applicants' claim 8. Therefore, this element is missing from both Annby and Tomalia. Since both references fail to teach a claimed element of Applicants' invention, a *prima facie* obviousness rejection cannot be maintained.

(2) There is no suggestion or motivation to modify or combine Annby and Tomalia

Annby and Tomalia also fail to suggest a reason to modify the urea side product containing composition of matter in order to produce a urea side product-free composition of matter. As mentioned above, neither Annby nor Tomalia teaches Applicants' element of a urea side product free composition of matter comprising a dendrimer with a subunit according to

claim 8. Since neither reference teaches this element, there is no motivation to modify Annby or Tomalia in order to produce the composition of matter of Applicants' invention. Therefore, the *prima facie* obviousness rejection cannot be maintained.

(3) The cited references do not provide a reasonable expectation of success

The cited references also fail to provide a reasonable expectation of success in performing the Applicants' invention. As mentioned earlier, neither Annby nor Tomalia suggests a urea side product free composition of matter comprising a dendrimer with a subunit according to claim 8. Since this is an element of Applicants' invention, and neither cited reference teaches this element, Annby and Tomalia cannot create a reasonable expectation that their methods can be successfully used to produce the composition of matter of Applicants' invention. Therefore, the *prima facie* obviousness rejection cannot be maintained.

Because the cited references fail to teach all the claimed elements, do not contain a suggestion or motivation to modify the reference teachings, and do not provide a reasonable expectation of success, a *prima facie* case of obviousness cannot be set forth. Thus, Applicants respectfully request the withdrawal of the rejection.

Appl. No. 09/963,858
Amdt. dated June 23, 2005
Reply to Office Action of February 23, 2005

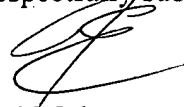
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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-442-1000.

Respectfully submitted,



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